



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/734,740

12/11/2003

Chung Shih

68936.001093

9514

1095

7590

03/30/2010

NOVARTIS  
CORPORATE INTELLECTUAL PROPERTY  
ONE HEALTH PLAZA 104/3  
EAST HANOVER, NJ 07936-1080

EXAMINER

FUBARA, BLESSING M

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

03/30/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/734,740	<b>Applicant(s)</b> SHIH ET AL.	
	<b>Examiner</b> BLESSING M. FUBARA	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 November 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. The examiner acknowledges receipt of request for extension of time, power of attorney, amendment and remarks, all filed 11/11/09. Claims 1, 4, 8, 9, 12, 18, 23, 29, 34 and 39 are amended. Claims 44-47 are canceled. Claims 1-473 are pending.

### ***Response to Arguments***

**Previous rejections that are not reiterated herein are withdrawn.**

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejections.

4. Claims 1, 4, 8, 9, 12, 18, 23, 29, 34 and 39 require that the polymeric composition remain free flowing upon parenteral administration at temperatures of between 35 and 42 °C . However, the instant specification is clear, that is, the composition remains free flowing within some temperature limits (see paragraphs [0013], [0017] an [0021]) as now recited in the amended claims but the administration is by intravenous and does not cover all aspects of parenteral administration such as subcutaneous (under the skin), and intramuscular (into muscle).

Art Unit: 1618

Thus, the administration is specific to intravenous and not to all aspects of parenteral administration. Therefore, the specification as filed does not envision polymeric composition such as the composition in claims 1, 4, 8, 9, 12, 18, 23, 29, 34 and 39 to remain free flowing when administered by all the parenteral routes.

5. The recitation of block co-polymer concentration of between 10-30% in claims 9, 14, 24, 30, 35 and 40 is also not envisioned.

### ***Response to Arguments***

6. Applicant's arguments filed 11/11/09 have been fully considered but they are not persuasive.

7. Applicant argues that the amendment to claims 9, 14, 24, 30, 35 and 40 overcomes the rejection.

8. The examiner disagrees because block co-polymer concentration of between 10-30% in claims 9, 14, 24, 30, 35 and 40 is also not envisioned by the specification as originally filed.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

Art Unit: 1618

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rath et al. (US 6,004,573) for reasons of record and reiterated herein below.

12. Rath discloses a water-soluble biodegradable ABA-type block copolymer drug delivery system having a gelation temperature at or below the body temperature (abstract, column 4, lines 57-65 and column 5, line 5), that is at body temperature the formulation is liquid and flowable meeting the limitation that the polymer solution is flowable at body temperature. Specifically Table 1 describes the behavior of the PLGA-PEG-PLGA tri-block polymer to gel above the gelation temperature. Rath discloses an average molecular weight ranging between from about 3,100 and about 4,500 for the block copolymer (abstract; Table 1; claims 1, 5, 12, 18) which is different from the recited range of 1500 to 3099 for the molecular weight requirements of claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 and the lower limit of Rath is very close to the upper limit of 3099; the block copolymer having about 51-83% by weight of hydrophobic A polymer block and about 17-49% by weight of hydrophilic B polymer block (abstract; column 5, lines 6-8) meeting claims 1, 4, 8, 12, 18, 23, 29, 34 and 39; the A block polymer consists of poly (lactide-co-glycolide) and the B block consists of polyethylene glycol (PEG) or polyethylene oxide (PEO) or polyoxyethylene; the lactate or lactide content of the A block is between about 65 and 85 mole percent and the glycolate or glycolide content in the A block is between about 15 and 35 mole

Art Unit: 1618

percent (column 5, lines 4-16) meeting claims 3, 6, 11, 17, 20, 32, 37 and 42. The A polymer block of Rathí is made from lactide and glycolide monomers (example 1), which meets the scope of claims 1, 2, 5, 10, 12, 16, 17, 18, 19, 23, 25, 29, 31, 34, 36, 39 and 41. “Free flowing liquid at body temperatures” recited in claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 is the property of the formulation/composition. The recitation in claims 1, 4, 8, 9, 12, 18, 23, 29, 34 and 39 that the composition remains free flowing liquid upon administration to a warm blooded animal at between 35 and 42 °C is the property of the composition and the composition of Rathí is capable of remaining free flowing when administered parenterally to a warm blooded animal at between 35 and 42 °C.

13. “Capable of solubilizing” as recited in the claims is the intended use of the composition. Claims 5, 10, 16 are product by process claims. Rathí teaches the method of claims 18 and 23 by providing the biodegradable polymer and parenterally administering the formulation the formulation (abstract, column 4, lines 63-65; column 5, lines 21-23). The method of claims 34 and 39 is the preparation of the polymer formulation and Rathí as described above and in Examples 6, 7 and 80

14. Rathí made the observation that ABA-type block copolymers that have hydrophobic A block copolymer content of between about 51-83% by weight and ABA block copolymer having a molecular weight of between about 3,100 and 4,500 are soluble in water at low temperatures and undergo reversible thermal gelation at mammalian physiological body temperatures (column 6, lines 32-40). Rathí specifically discloses that the ABA-type block polymer composition gels at body temperature, which is 37 °C (abstract and column 1, lines 19-21) and this means that between 35 °C and 36.999 °C, the ABA-type polymeric composition of Rathí is a liquid. Rathí

Art Unit: 1618

discloses that the concentration of the soluble block copolymer at below the gelation temperature is the functional concentration which ranges from 3% to 50% (column 9, lines 55-65) and the concentration of the block copolymer is related to the sol-gel phase transition of the polymer as a function of temperature (column 9, lines 63-67 and Figure 1).

15. The biodegradable drug delivery system of Rathie is an aqueous solution of the ABA block copolymer and dissolved drug or drug as a suspension or emulsion, the drug delivery system is administered parenterally, topically, transdermally or inserted into ocular, vaginal, rectal, nasal, oral and transurethral cavities; the drug makes up between 0.01 to 20% by weight of the of the drug delivery formulation (column 10, lines 19-65 and claims 12-18) and parenteral means intramuscular, intraperitoneal, intra-abdominal, subcutaneous, intravenous and intra-arterial (column 5, lines 22-24). Rathie specifically teaches a method of administering a drug to a warm blooded animal in a liquid form below the gelation temperature (claim 1) and in Rathie the gelation temperature is the physiological temperature of the warm blooded animal, which is 37 °C (abstract), since the instant method of claims 18 and 23 administer instant composition to warm blooded animals, the method of Rathie meets the scope of the instant method claims 18 and 23.

16. Rathie specifically teaches that the block copolymer increases solubility and chemical stability of many drugs (column 10, line 66 to column 11, line 28) and polyols including sugars, amino acids, surfactants, polymers, proteins and certain salts can be incorporated into the block copolymer as additives (column 12, lines 4-11) and amino acids and certain salts can be buffer. Thus the composition of Rathie comprises excipients meeting the scope of instant claim 13.

Art Unit: 1618

17. The instant invention is directed to block copolymeric composition comprising block copolymeric carrier and a drug with the proviso that when the copolymer is an aqueous solution, the copolymeric composition is a liquid at temperatures at body temperatures. The instant polymeric composition encompasses the polymeric composition of Rath i in light of the discussion following.

18. The functional concentration of the biodegradable copolymer in instant claims 9, 14, 24, 30, 35 and 40 is between 10-30%. In Rath i, the functional concentration of the biodegradable copolymer is from about 3% to about 50%, which overlaps the instant range of 10-30 and points within Rath i's disclosed range intersects points within the recited range, Rath i's functional concentration at those points meets the scope of the instant functional concentration range. The lactide or lactic acid content of the A block ranges from 20 to 100 mole percent and the glycolide or glycolic acid ranges from 0 to 80 mole percent in instant claims 3, 6, 11, 17, 20 and 26. The lactate or lactide content is between about 65 to 85 mole percent and glycolate or glycolide content is between 15 and 35 mole percent in the A block in Rath i and these ranges lie within the instant ranges. Thus Rath i's ranges in the content of lactate or lactide and glycolate or glycolide meet the scope of the instant ranges. The method of administering in the prior art meets the scope of the administration method of instant claims 18, 22, 23 and 28. Regarding claims 7, 15, 21 and 27, the instant drug content of  $10^{-6}$  to 100% encompasses the narrower drug content range of 0.01 to 20% or the preferred range of 0.01% to 10% disclosed in Rath i, and Rath i meets the scope of the instant drug content.

19. Rath i in column 12, line 66 to column 13 line 10 exemplifies a specific ABA block copolymer that comprises 75% by weight hydrophobic A block of PLGA and 25% by weight

Art Unit: 1618

hydrophilic B block of PEG, ABA block copolymer that has an average molecular weight of 4000, 75% mole percent lactate or lactide and 25 mole percent glycolate or glycolide. Although Rath teaches the preparation of the above specific PLGA-PEG-PLGA tri-block copolymer, Rath broadly discloses block copolymer having about 51-83% by weight of hydrophobic A polymer block and about 17-49% by weight hydrophilic B polymer block.

20. Since the hydrophobic A polymer block in Rath ranges from 51-83% and the hydrophilic B polymer block ranges from 17-49% and since these ranges are covered in the ranges of the instant A and B block, there are points within those ranges where the percent amounts of the A and B blocks of the instant claims and the prior art are the same. This is true also for the mole percent of the lactide and glycolide, for the molecular weight of the block copolymer and for the drug content in the polymeric composition. Thus, at those points when they are the same the polymeric compositions of the prior art and the invention are the same and thus the properties would be the same. Thus, the polymeric compositions of the invention and the prior art would have the same property. Specifically, the gelation properties of both compositions would be the same and there is nothing in the instant claims that indicates that the properties are not. It appears that there is an aspect of applicants' invention that allows the composition to remain liquid at above body temperature and applicants have not communicated that in the claims.

21. The molecular weight of the polymer in Rath is different from that of the claims. But a molecular weight of 3100 and 3099 are quite close. Applicant has not provided factual showing that the recited molecular weight range provides unexpected results. Therefore, taking teachings of Rath, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that using polymer having molecular weight in the range

Art Unit: 1618

disclosed by Rathí would produce the expected composition that is solution at temperatures of between 25 °C and 37 °C. The disclosed range is indicative that the molecular weight is variable and as such polymers having different molecular weight may be used with the expectation of obtaining thermal reversible composition.

***Response to Arguments***

22. Applicant's arguments filed 11/11/09 have been fully considered but they are not persuasive.

23. Applicant on pages 13-17 argues that Rathí does not expressly or inherently describe all the limitations of amended claims 1-43, that the examiner incorrectly states that free flowing liquid at body temperatures is a property of the composition, that Rathí does not teach molecular weight of between 1500 and 3099 Da, that 3100-4500 cannot anticipate 1500-3099, that the polymeric composition of Rathí under goes reverse thermal gelation.

24. The examiner disagrees that Rathí cannot render obvious the claimed invention because  
a) Reverse thermal gelation at body temperature is composition that is liquid before the body temperature is reached and at administration is a gel at body temperature. b) The claims are directed to composition and the interpretation that the composition is free flowing at temperatures of between 35 and 42 °C is a property of the composition is correctly interpreted; The claims have not recited a liquid but even if the claims did, composition of Rathí is a liquid at temperatures below body temperature, which is 37 °C; 35 °C is below 37 °C. c) The rejection was made under 35 USC 103 in the alternate so that while the examiner agrees with the applicant that a molecular weight of 3100 to 4500 cannot anticipate a molecular weight of 1500 to 3099, it was stated in the rejection that the lower limit of 3100 renders obvious the upper limit of 3099

Art Unit: 1618

and about 3100 allows for molecular weight of slightly lower than 3100 which renders obvious the claimed upper limit.

25. The genus of 3% to about 50% renders obvious the species of 10-30% in claims 9, 14, 24, 30, 35 and 40.

### ***Double Patenting***

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 1-43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-77 of U.S. Patent No. 6201072 respectively. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not

Art Unit: 1618

identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated, or would have been obvious, over the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the prior issued patents use and make the same formulation. Although, the issued claims say reverse thermal gelation, it is noted that the issued composition is also free flowing when administered.

### ***Response to Arguments***

28. Applicant's arguments filed 3/12/09 have been fully considered but they are not persuasive.

29. Applicant's argument that the interpretation that the composition undergoing reverse thermal gelation cannot be free flowing at a temperature of 35 °C is not persuasive because at 35 °C the composition is not a gel but a liquid except applicant wants to equate 35 °C as body temperature.

30. Applicant also argues that one cannot modify molecular weight of between 2000 and 4900 of the patent to 1500-3099.

31. The examiner disagrees with applicant's interpretation because molecular weight of 2000 to 4990 overlaps the claimed molecular weight of 1500 to 3099 and "where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Art Unit: 1618

32. The claims of 6,201,072 and the disclosure of Rathí do not teach away from the instant claims.

33. No claim is allowed.

34. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

35. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday-Friday from 7:30 am to 3:30 pm.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Art Unit: 1618

38. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-8253.

/Blessing M. Fubara/

Primary Examiner, Art Unit 1618